Ejaculation Disorders

Ejaculation—The Long and Short of It

Reviewed by Jacob Rajfer, MD
Department of Urology, University of California at Los Angeles, Los Angeles, CA

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Tramadol HCL Has Promise in On-Demand Use to Treat Premature Ejaculation

Salem EA, Wilson SK, Bissada NK, et al.

J Sex Med. 2008;5:188-193.

During the past decade, the majority of investigative studies related to sexual dysfunction have revolved around erectile dysfunction (ED). Very little attention has been paid to one of the stepsisters of ED, disorders of ejaculation. This is surprising because the only sexual disorder more common than ED is premature ejaculation. It is estimated that about 33% of men complain of premature or early ejaculation and, unlike ED, it is not age related—there is a high prevalence regardless of age. Although the mechanisms involved in the ejaculatory process are well known, what causes a man to have an early ejaculation response remains a mystery. Some have hypothesized that because so many men have this physiologic complaint, early ejaculation may not be a disorder at all and may represent normal function for many men. However, many men seek treatment for this condition. Thus, there seems to be a clinical need for a regimen that would allow some men to prolong their time to ejaculation.

At present, there are no US Food and Drug Administration–approved drugs to treat this complaint. Anecdotal reports support the clinical observations of many investigators and clinicians that selective serotonin reuptake inhibitors (SSRIs) can delay ejaculatory time, although there are no randomized, controlled trials to unequivocally support this contention. SSRIs, although potentially effective for some men with early or premature ejaculation, do come with a host of side effects (some sexual), and the timing as to when to take these drugs to prevent the ejaculatory dysfunction is debatable. Recently, there was an anecdotal report that tramadol, an anti-inflammatory agent with minimal side effects, was effective at the 50-mg oral dose in improving ejaculatory function when taken 1 to 2 hours prior to sexual activity.[1] To this end, Salem and colleagues recently published a report on their single-blind, placebo-controlled, crossover study on 60 patients with documented early or premature ejaculation using 25 mg of tramadol. They showed that the drug improved intravaginal ejaculation latency time by more than 5 minutes. Based on their observations, the authors concluded that 25 mg of tramadol taken orally 1 to 2 hours prior to sexual activity should replace SSRIs as the standard first-line treatment of men with early or premature ejaculation. ■

Reference

1. Safarinejad MR, Hosseini SY. Safety and efficacy of tramadol in the treatment of premature ejaculation: a double-blind, placebo-controlled, fixed-dose, randomized study. *J Clin Psychopharmacol.* 2006;26:27-31.

Incontinence

Stress Incontinence and Prolapse Therapy Assessment

Reviewed by Dmitriy Nikolavsky, MD, Michael B. Chancellor, MD
Department of Urology, William Beaumont Hospital, Royal Oak, MI

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Over 200 million people worldwide have urinary incontinence. The most common type of urinary incontinence is stress urinary incontinence (SUI); increasing parity, advanced age, and obesity are known risks for acquiring the condition. Trauma to the pelvic floor musculature, connective tissue, or nerves later in life becomes the most important risk factor for development of SUI. The following studies examine outcomes of surgical treatments of SUI.

Two-Year Outcomes After Surgery for Stress Urinary Incontinence in Older Compared With Younger Women

Richter HE, Goode PS, Brubaker L, et al.

Obstet Gynecol. 2008;112:621-629.

This prospective analysis of the Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr) aimed to determine whether age may affect perioperative and postoperative

outcomes of anti-incontinence surgery, namely Burch colposuspension and placement of a pubovaginal sling. Investigators compared women older than 65 years with those younger than 65 years for baseline characteristics, adverse events, and 2-year outcomes after the procedure. Additionally, multivariable analyses were performed for age and for the outcome variables that were different in univariable analysis.

The subjects of the study were 655 women who were included in analyses of perioperative events, of which 520 were included in the 2-year outcome analysis. The older group included 81 women with a mean age of 69 years, whereas the younger group consisted of 574 women with a mean age of 49.4 years. Not surprisingly, the groups differed in medical, surgical, obstetric, and social history. For example, older women were more likely to have stage 3 or 4 pelvic organ prolapse.

Analysis of perioperative outcomes demonstrated no significant difference in time to normal voiding in the older group compared with the younger group (14 days vs 11 days; $P = .42$), but a slightly longer time to normal activities in the older group (50 days vs 42 days; $P = .05$). Additionally, perioperative adverse events and length of stay did not differ between the 2 groups. The 2-year outcome analysis yielded worse results for the older group. The older group was more likely to have a positive stress test at the time of follow-up. Furthermore, the older women were more likely to undergo repeat surgical treatment of SUI.

The NIH team concluded that perioperatively older women undergoing Burch colposuspension or placement of a pubovaginal sling for SUI are faring just as well as younger women. However, 2-year outcomes are expected to be worse in older women.

Two-Year Outcomes After Sacrocolpopexy With and Without Burch to Prevent Stress Urinary Incontinence

Brubaker L, Nygaard I, Richter HE, et al.

Obstet Gynecol. 2008;112:49-55.

This study was a part of the Colpopexy and Urinary Reduction Efforts (CARE) trial that aimed to determine outcomes after sacrocolpopexy alone or in combination with Burch colposuspension. The outcomes in question included voiding symptoms, pelvic symptoms, and pelvic support. The subjects included in this study were stress-continent women undergoing sacrocolpopexy who were randomized to receive or not to receive simultaneous Burch colposuspension. The researchers and the patients were blinded to the assigned treatment at least 3 months postoperatively. The patients were evaluated with standardized pelvic organ prolapse examination and pre- and postoperatively were followed with the Pelvic Floor Distress Inventory and the Pelvic Floor Impact Questionnaire. The duration of follow-up was 2 years and the stress incontinence endpoint was defined as presence of stress incontinence symptoms, positive cough stress test, or interval treatment of stress incontinence.

Of the original randomized 322 participants, 302 were followed for 2 years. Two years after the surgery, 32.0% of women in the Burch group developed stress incontinence, compared with 45.2% in the control group ($P = .026$). Additionally, the Burch group showed a trend toward fewer urgency symptoms (32.0 vs 44.5% in the control group; $P = .085$). In 95% of patients in both groups the apex was well supported, as defined by point C being within 2 cm of total vaginal length ($P = .18$). This meant that apex support was not affected by concomitant Burch colposuspension.

As concluded by the multicenter research team, the early advantage of prophylactic Burch colposuspension for SUI seen at 3-month follow-up was persistent at 2 years. The high success rate of apical anatomic support was not affected by concomitant Burch colposuspension. In conclusion, the authors recommended prophylactic Burch colposuspension at the time of sacrocolpopexy for women with mobile urethra.

Retraction–Autologous Myoblasts and Fibroblasts for Treatment of Stress Urinary Incontinence: A Randomised Controlled Trial

Kleinert S, Horton R.

Lancet. 2008;372:789-790.

This article is a retraction in relation to the earlier publication in *The Lancet* by Dr. Strasser and colleagues, researchers from the Medical University of Innsbruck, Austria (*Lancet*. 2007;369:2179-2186). The original study, dated June 30, 2007, compared injections of autologous myoblasts and fibroblasts with alternative injection of collagen for treatment of SUI. The study was flawed by multiple ethical and legal violations. This is a sad development in an exciting area of urologic research: adult stem cells for treatment of SUI.

The Austrian government identified multiple irregularities in the study. Based on this, journal editors decided to retract the article from the published record. In the September 6 issue of *The Lancet*, its senior executive editor Sabine Kleinert, MD, and editor/publisher Richard Horton stated that the investigation "raise(s) doubts as to whether a trial as described in *The Lancet* ever existed."

The first concern regarding this study was expressed in the February 9, 2008 issue of *The Lancet,* when the editors published a correction related to the original article's conflict of interest statement. Several of the coauthors had a relationship to the company funding the research, Innovacell Biotechnologie. In April 2008, the Austrian Ministry of Health initiated an investigation regarding ethical approval and conduct of the research. In their retraction, *The Lancet* editors cited the conclusion of the Austrian inspectors, saying "the study was conducted neither according to Austrian law nor according to the standards of the International Conference on Harmonization of Good Clinical Practice." Among the violations the government inspectors found were critical deficiencies in the process for obtaining patient consent, documenting the source data, and getting approval of the ethics committee. Inspectors found at least 1 forged patient signature, and other key documents existed only as copies, rather than originals. Some of the documents "existed in different unsigned and undated versions." ■